REMARKS

This paper responds to the Final Office Action dated May 11, 2009.

Status of Claims

No claims are amended, no claims are canceled, and no claims are added. As a result, claims 1-4 are now pending in this application.

No new matter is added.

I. Claims 1-4 were rejected under 35 U.S.C. § 102(b) for anticipation by Gronvald et al. (U.S. Patent No. 5,010,090). The Office Action states "Applicant has not shown that the solid form produced in the reference is different from the form instantly claimed."

Applicants are also enclosing a **Rule 132 Declaration** and **Exhibits I, II** and **III** in response to arguments made in the Office Action of May 11, 2009.

Exhibit I is a copy of the experimental details for recrystallizing tiagabine hydrochloride from ethyl acetate. The recrystallization was carried out under the direction of Dr. K Srinivasu, Senior Manager of Organic Synthesis at Sun Pharmaceutical (Applicant). This exhibit is described in Points Number 7 and 8 of the **Rule 132 Declaration** of Dr. K. Srinivasu.

Exhibit II is a copy of a letter from Professor T. N. Guru Row at the Indian Institute of Science and describes his attempts to obtain XRD data for sample 7022 (Batch No. 7022/F/691/32A2) of tiagabine hydrochloride recrystallized from ethyl acetate. This exhibit is described in Point Number 9 of the **Rule 132 Declaration** of Dr. K. Srinivasu.

Exhibit III is a copy of a second letter from Professor T. N. Guru Row at the Indian Institute of Science and describes his comparison of the XRD pattern of tiagabine hydrochloride 7022 (Batch No. 7022/F/691/32A2) recrystallized from ethyl acetate with that of the simulated pattern of tiagabine hydrochloride Polymorph IV, prepared as described in the present patent application. This exhibit is also described in Point Number 9 of the **Rule 132 Declaration** of Dr. K. Srinivasu.

Applicants appreciate that all previous rejections under 35 U.S.C. § 112, 1st paragraph enablement; 35 U.S.C. § 112, 2nd paragraph; and 35 U.S.C. § 102 rejections over Ahrndt et al. and Anderson et al. have been withdrawn. Although not explicitly mentioned in the Office Action, Applicants believe that the previous rejections under 35 U.S.C. § 103(a) over Ahrndt et al. and Anderson et al. have also been withdrawn.

Rejections of Claims Under 35 U.S.C. §§102(b)

I. The Office Action maintains the rejection of claims 1-4 under 35 U.S.C. § 102(b) as anticipated by Gronvald et al. (U.S. Patent No. 5,010,090). The Office Action asserts that Applicants have not shown that the solid formed produced by Gronvald et al. is different from their crystal form of tiagabine hydrochloride.

Applicants traverse this rejection and provide the following arguments to support their belief that tiagabine hydrochloride Polymorph IV is different from the tiagabine hydrochloride described by Gronvald et al.

Gronvald et al. is not enabling. The reference does not describe the recrystallization of tiagabine hydrochloride from ethyl acetate.

The Office Action maintains the rejection over Gronvald et al (U.S. 5,010,090). The reasons for this rejection are given in the previous Office Action of August 29, 2008. There, Office Action alleged that Gronvald et al. "teaches a solid form of the claimed compound which is isolated from ethyl acetate (see columns 9 and 10)." The current Office Action requests Applicants show that the solid formed produced by Gronvald et al. is different from their crystal form of tiagabine hydrochloride.

A careful reading of the footnotes to Table I, in columns 9 and 10 of Gronvald et al indicates that compounds labeled with a "*" were crystallized from ethyl acetate, isopropanol, acetone, or water. Gronvald et al. is silent as to which solvents were used successfully to recrystallize which compounds. The disclosure in Gronvald et al. about recrystallization of tiagabine from ethyl acetate is limited to the description in the footnotes.

Furthermore, when Applicants attempted to recrystallize tiagabine hydrochloride from ethyl acetate, they obtained an impure product whose crystal structure could not be determined. See Points Number 7 and 8 of the enclosed **Rule 132 Declaration** of Dr. K. Srinivasu.

Applicants provide a showing that tiagabine hydrochloride Polymorph IV differs from that of the polymorph disclosed in Gronvald et al. (the '090 patent).

The Office Action requests that Applicants provide a showing of how their claimed Polymorph IV differs from that of the polymorph disclosed in Gronvald et al. (the '090 patent).

Examiner's attention is directed to the enclosed **Declaration under 37 C.F.R. 1.132** paragraphs 7 and 8, where Dr. K. Srinivasu declares that under his direction, his laboratory attempted to recrystallize tiagabine hydrochloride from ethyl acetate and found that it required an inordinately large amount of solvent, and gave tiagabine hydrochloride that was brown in color and had a blue tinge. The color of this product was different from that of samples of tiagabine hydrochloride Polymorph IV prepared as described in the Applicants' patent application. The experimental conditions for the recrystallization of tiagabine hydrochloride from ethyl acetate are provided in **Exhibit I**.

Examiner's attention is further directed to the enclosed **Declaration under 37 C.F.R. 1.132** paragraph 9, and **Exhibit II**, where Dr. K. Srinivasu declares that a sample of the tiagabine hydrochloride, prepared by recrystallization from ethyl acetate, was submitted to Professor T. N. Guru Row for XRD analysis. Professor Guru Row attempted to obtain XRD data for the sample so that it could be compared with Applicants' sample of tiagabine hydrochloride Polymorph IV as disclosed and claimed in the present patent application, U.S. Serial No. 10/583,805. As can be seen from Professor Guru Row's letter, "Attempts to obtain a unique indexing on the pattern failed as we perceive that there is more than one phase associated with the sample or the sample is contaminated with impurity peaks." Professor Row's letter clearly indicates that the tiagabine hydrochloride, obtained, by recrystallization from ethyl acetate, is not pure.

Examiner's attention is further directed to the enclosed **Declaration under 37 C.F.R. 1.132** paragraph 9, and **Exhibit III**, where Dr. K. Srinivasu declares that Professor Guru Row compared the recorded XRD pattern of tiagabine hydrochloride, (Batch No.

7022/F/691/32A2) recrystallized from ethyl acetate, with that of the simulated pattern of tiagabine hydrochloride Polymorph IV, prepared as described in the present patent application. Professor Row's letter clearly indicates that the tiagabine hydrochloride, obtained by recrystallization from ethyl acetate, is not the same as the new and previously unknown tiagabine hydrochloride Polymorph IV claimed in the present U.S. Patent Application Serial No. 10/583,805.

The prior art of record also teaches that ethyl acetate is a poor choice as a solvent for recrystallizing tiagabine hydrochloride.

Applicants also direct the Examiner's attention to U.S. Patent 5,958,951 (Arndt et al.) cited on page 1 of the present Application and submitted in the IDS filed August 25, 2006. At column 1, line 39-49, the '951 patent states "The alternative product, which is disclosed in the U.S. Pat. No. 5,010,090 (column 8, line 62) [Gronvald et al.] can only be prepared through a labor-intensive process as described, using ethyl acetate. Furthermore, analysis has shown that products manufactured by this process contain unwanted amounts of the crystallizing solvent. Other organic solvents may be used in the isolation of the product, but organic solvents will often form chlathrates, i.e. solvates of tiagabine hydrochloride and the resp. organic solvent." Applicants believe that this disclosure in U.S. 5,958,951 provides further showing that Applicants' tiagabine hydrochloride Polymorph IV cannot be the same polymorph obtained by Gronvald et al. by recrystallization from ethyl acetate – if in fact it was actually recrystallized from ethyl acetate as noted above.

Applicants further direct the Examiner's attention to U.S. Patent 5,354,760 (Petersen et al.) cited on page 1 of the present Application and submitted in the IDS filed August 25, 2006. At column 1, lines 33-51 the '760 patent discloses that tiagabine hydrochloride can be recrystallized from ethyl acetate (citing the Danish equivalent of Gronvald et al. above). At column 1, lines 46-48, the '760 patent states "Furthermore analysis has shown that products manufactured by this process contain unwanted amounts of the crystallizing solvent ethyl acetate." Additionally, at column 1, lines 49-52, the '760 patent continues, "Use of alternative organic solvents such as acetonitrile, butyl acetate, toluene, acetone, dichloromethane etc. also gives products containing various amounts of the used crystallizing solvent." The '760 patent

further discloses at column 1, line 67 to column 2, line 1, "It has now been found that water can be used as a crystallizing solvent for this compound giving very reproducible results of a monohydrate crystal form." Applicants believe that these disclosures in U.S. 5,354,760 provide additional showings, as requested in the Office Action, that Applicants' tiagabine hydrochloride Polymorph IV cannot be the same polymorph obtained by Gronvald et al. by recrystallization from ethyl acetate.

Additional remarks.

Furthermore, both Arndt et al, and Petersen et al. teach that recrystallization of tiagabine hydrochloride from ethyl acetate results in a product containing a large amount of solvent. A large amount of solvent would be expected to result in any crystals formed having different unit cell parameters and XRD peaks than those recited in Applicants' claims.

CONCLUSION

Applicants believe that the above remarks provide the showing requested in the Office Action that tiagabine hydrochloride Polymorph IV differs from that described in Gronvald et al. Applicants believe that the above remarks fully address the rejection of claims 1-4, under 35 U.S.C. §§102(b) as anticipated by over Gronvald et al. Reconsideration withdrawal of the rejection of claims 1-4 is respectfully requested.

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone

Applicant's representative at (612) 373-6961 to facilitate prosecution of this application. If necessary, please charge any additional fees or deficiencies, or credit any overpayments to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 8 day of July, 2009.

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